Supplementary Materials: Letermovir for Cytomegalovirus Prophylaxis in Lung Transplant Patients with Valganciclovir-Induced Leukopenia

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Table S1. Detailed patient demographics.

Patient	Age	Sex	Tx indication	Tx type	CMV status	Leukopenia episodes prior to LET	Median leukopenia duration (d)	WBC nadir (K/uL)	Time to leukopenia resolution after LET (d)	Indication for CMV prophylaxis w/ LET	LET start (POD)
#1	27	M	CF	BLT	D+/R−	4	7	0.61	44	Primary	102
#2	65	F	CF	BLT	D+/R−	5	11	0.62	9	Secondary	182
#3	62	F	IPF	BLT	D+/R−	6	21	1.17	8	Secondary	279
#4	54	F	IPF	BLT	D+/R+	4	8	1.03	6	Primary	99
#5	63	M	IPF	BLT	D+/R−	2	92.5	0.94	33	Primary	294
#6	65	F	IPF	SLT	D+/R−	7	23	1.24	38	Secondary	767
#7	49	M	CF	BLT	D+/R−	2	58	1.10	10	Primary	321
#8	62	F	COPD	BLT	D+/R−	4	29.5	1.48	7	Secondary	601
#9	56	F	COPD	BLT	D-/R+	4	23	1.11	14	Secondary	219
#10	68	M	IPF	BLT	D+/R−	4	13	2.00	8	Primary	185
#11	68	M	IPF	BLT	D-/R+	1	29	1.10	13	Primary	77
#12	64	M	COPD	BLT	D+/R−	4	5	<0.30	5	Secondary	118
#13	60	F	COPD	SLT	D+/R−	2	136	0.90	56	Secondary	515
#14	60	M	CLAD	BLT	D-/R+	1	34	2.19	7	Primary	101
#15	27	M	CF	BLT	D-/R+	1	112	0.90	34	Primary	154
#16	62	M	IPF	BLT	D+/R+	2	16.5	0.59	−6*	Primary	110
#17	40	M	Sarcoidosis	BLT	D+/R−	1	184	1.40	77	Secondary	263

Leukopenia episodes were defined as WBC <4 K/uL on consecutive blood samples collected at least 1 day apart. Resolution of leukopenia was defined as WBC ≥ 4K/uL on two consecutive blood samples collected at least 1 day apart. BLT, bilateral lung transplant; CF, cystic fibrosis; CLAD, chronic lung allograft dysfunction; COPD, chronic obstructive pulmonary disease; IPF, idiopathic pulmonary fibrosis; LET, letermovir; LT, lung transplant; POD, post-operative day; SLT, single lung transplant; Tx, transplant. * = Patient #16 had resolution of leukopenia 6 days prior to starting letermovir.

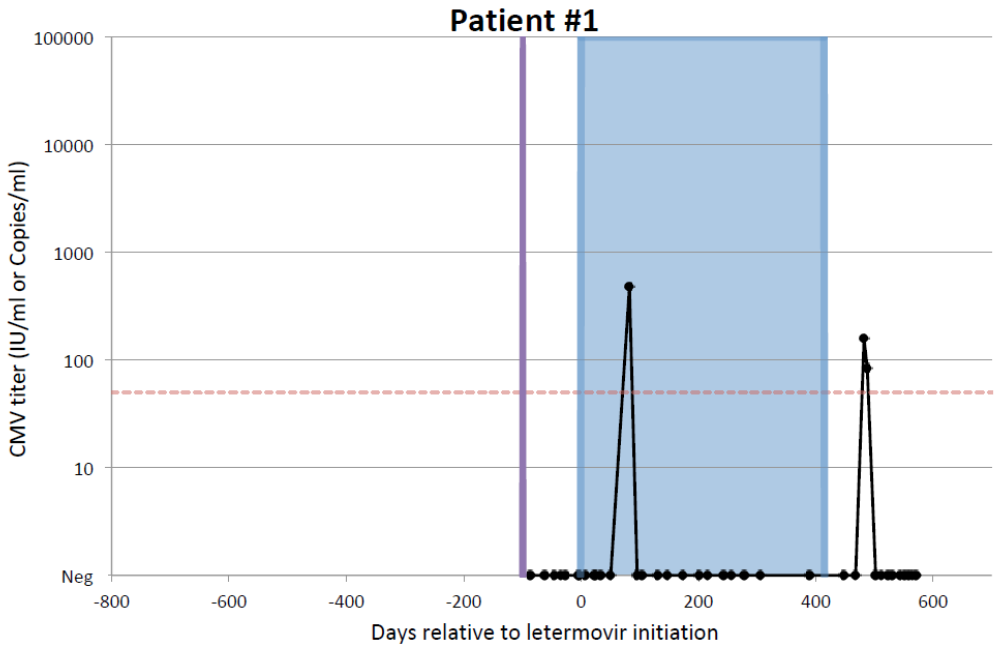
Table S2. Repeated Measures Mixed Model.

Description	Parameter	Parameter Estimate	p-value
Intercepts	Valganciclovir	9.20	0.0449
	Letermovir	7.51	
Slopes	Days Post-Transplant for No Letermovir Yet	−0.0113	<0.0001
	Days Post-Transplant for Letermovir	−0.0043	

Table S3. Laboratory values and filgrastim doses measured or administered before and after letermovir.

Patient #	WBC Pre (K/uL)	WBC Post (K/uL)	SCr Pre (mg/dL)	SCr Post (mg/dL)	Tacrolimus Pre (ng/mL)	Tacrolimus Post (ng/mL)	Filgrastim doses Pre	Filgrastim doses Post
1	3.43	3.05	1.55	2.30	8.20	9.20	8	2
2	2.86	4.24	0.98	0.98	8.00	7.90	3	0
3	3.06	4.85	2.15	1.85	5.40	4.60	1	0
4	2.61	4.76	0.62	0.65	10.45	10.40	11	0
5	2.00	4.60	4.40	3.57	9.70	5.25	6	0
6	4.70	6.05	1.50	2.45	7.80	14.45	3	0
7	2.20	7.55	1.25	1.20	10.18	7.70	2	0
8	5.00	7.71	1.51	1.35	6.70	9.60	5	0
9	1.60	2.90	2.29	1.90	11.90	5.00	17	0
10	4.24	8.47	1.66	1.65	8.30	9.10	0	0
11	4.60	4.48	1.00	0.96	11.35	11.40	0	2
12	4.80	7.77	1.12	0.97	7.60	8.60	9	7
13	2.80	4.50	1.48	1.21	7.50	3.50	6	0
14	4.59	5.91	2.28	3.60	7.65	7.80	0	2
15	1.19	5.20	1.10	1.25	12.00	9.55	4	0
16	2.62	5.57	1.16	1.27	8.80	10.60	8	0
17	2.42	3.09	1.00	1.22	8.50	15.20	0	0

WBC significantly increased following letermovir initiation (3.15 K/uL pre-letermovir vs. 5.46 K/uL post-letermovir, $p<0.0001$). There was no significant change in SCr or tacrolimus trough level after starting letermovir ($p=0.56$ and 0.48, respectively). Mean number of filgrastim administrations required to maintain normal WBC levels were significantly lower following initiation of letermovir (4.88 doses pre-letermovir vs. 0.76 doses post-letermovir, $p=0.003$). SCr, serum creatinine.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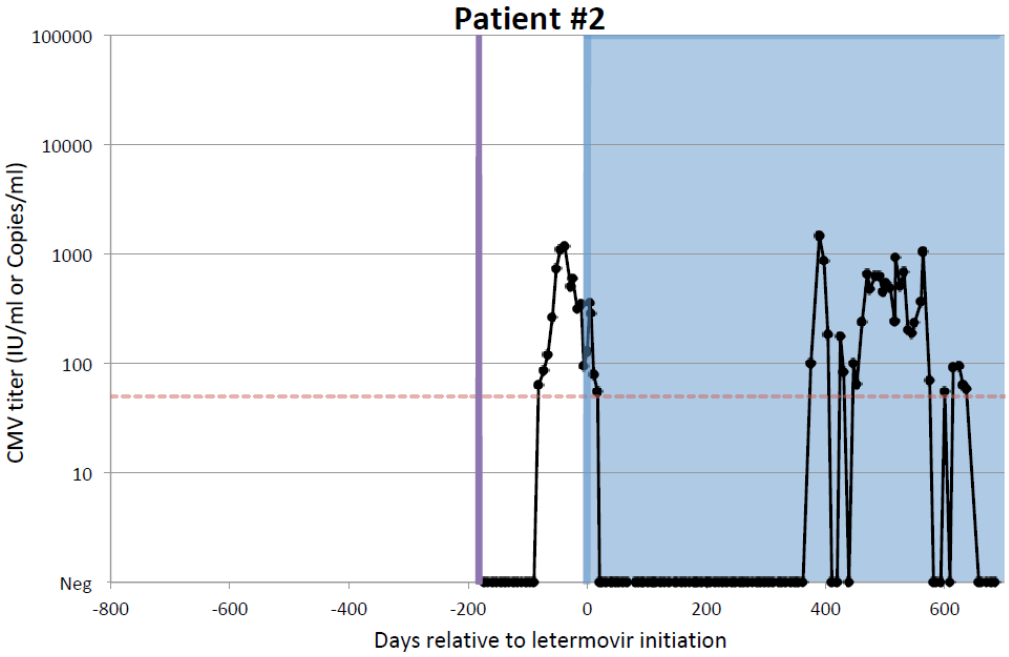
600
Days relative to letermovir initiation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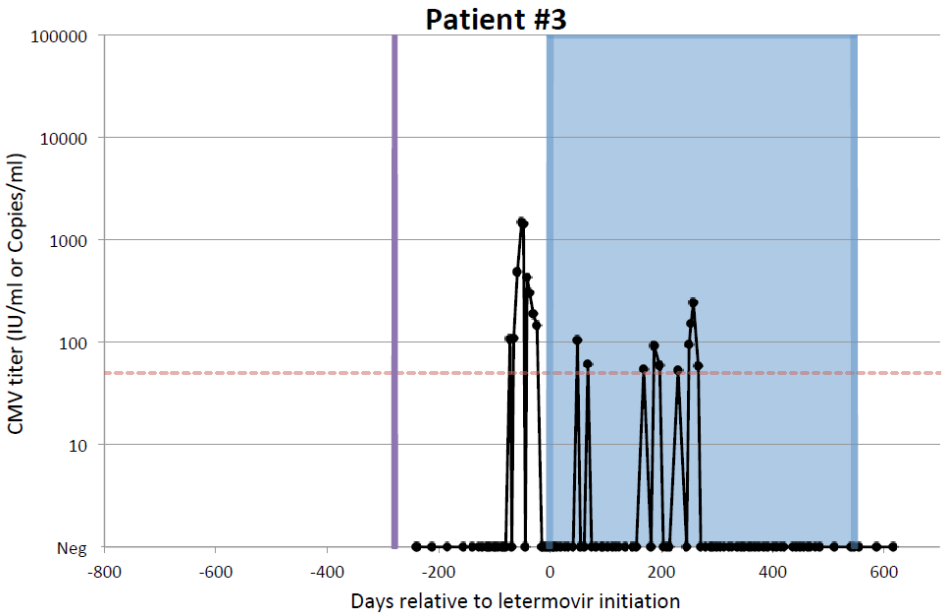
Days relative to letermovir initiation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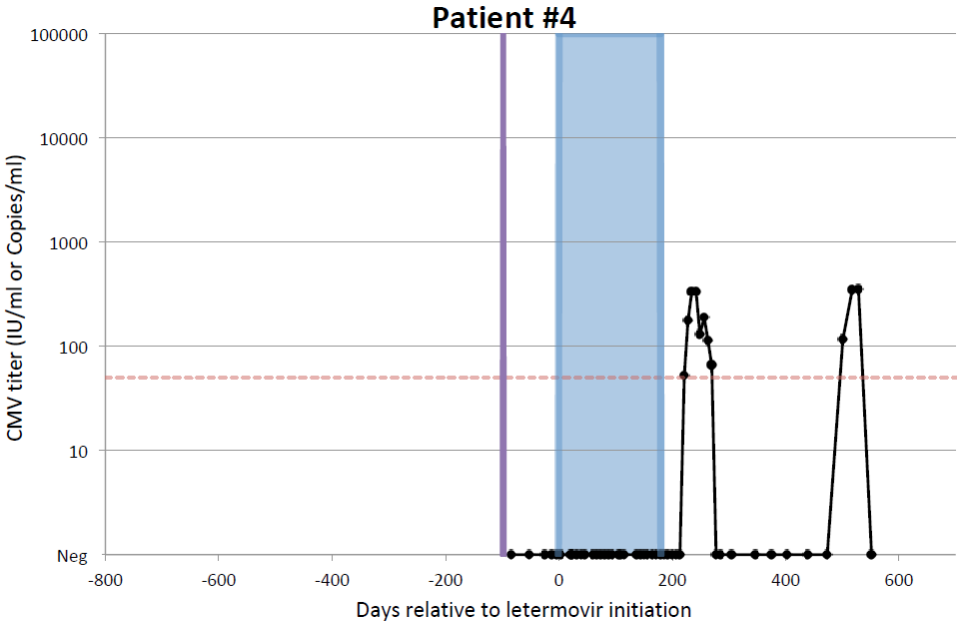
Days relative to letermovir initiation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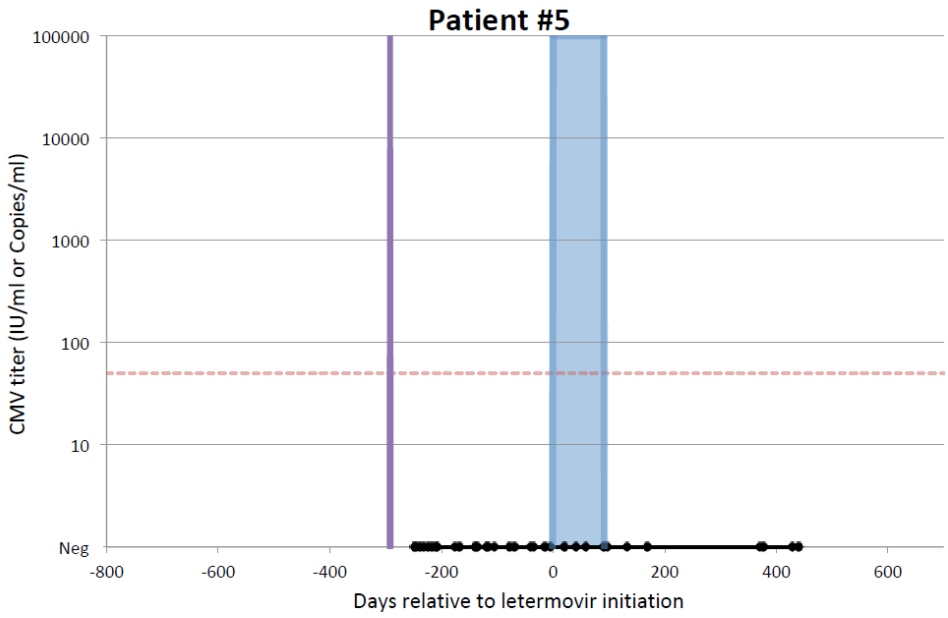
Days relative to letermovir initiation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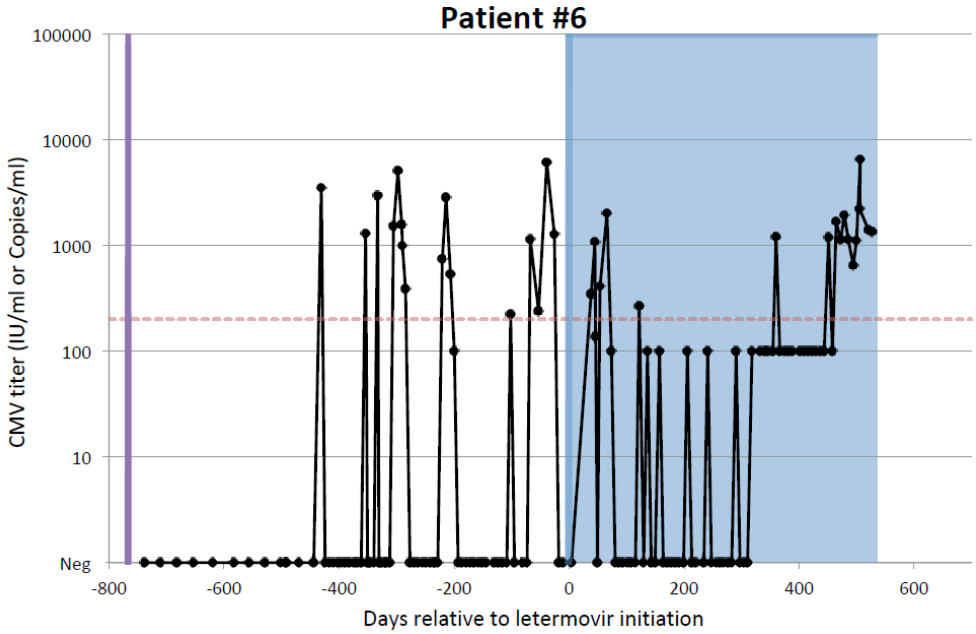
600
Days relative to letermovir initiation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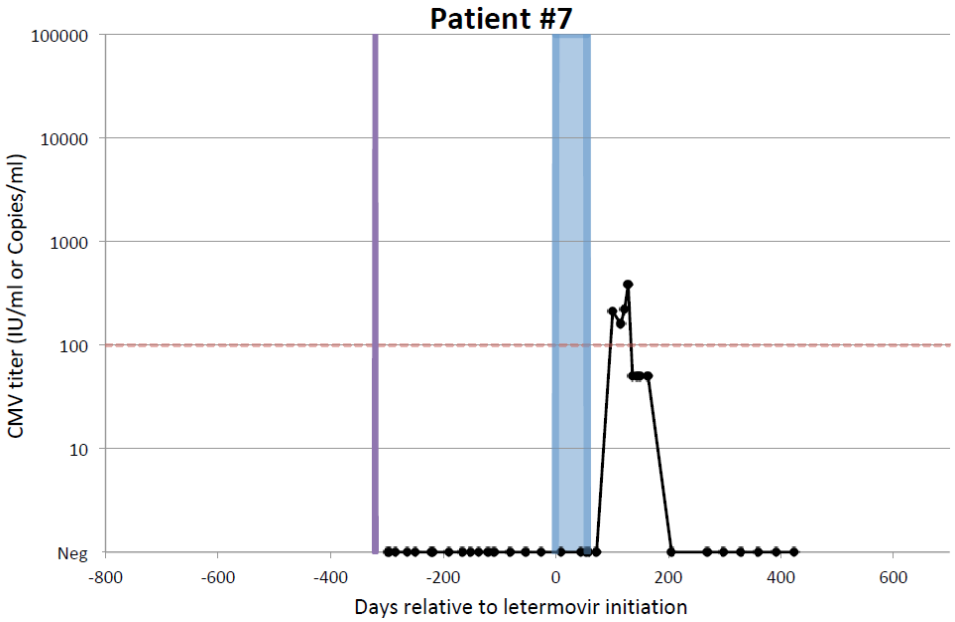
600
Days relative to letermovir initiation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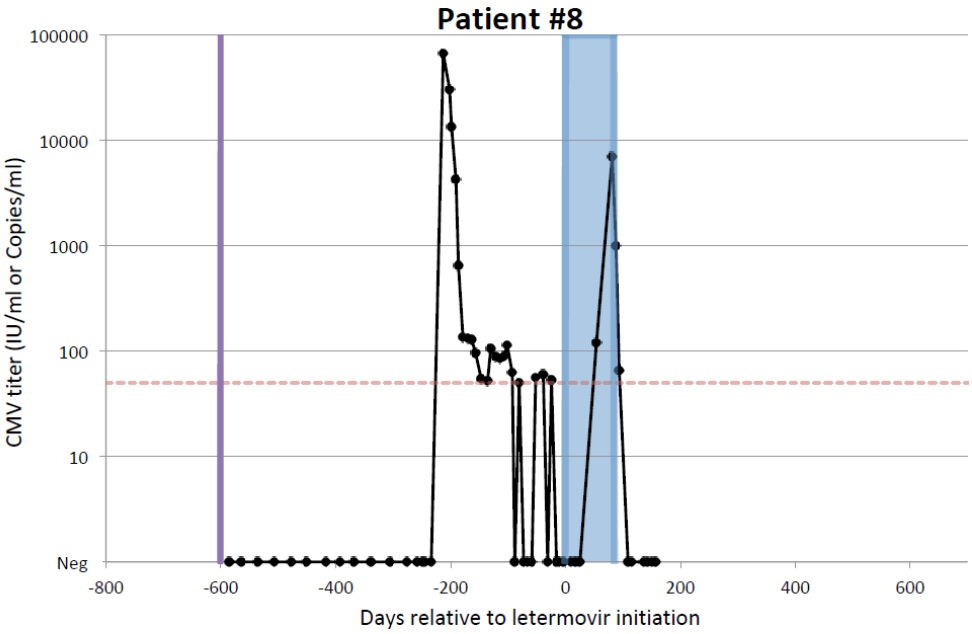
400
600
Days relative to letermovir initiation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CMV titer (IU/ml or Copies/ml)
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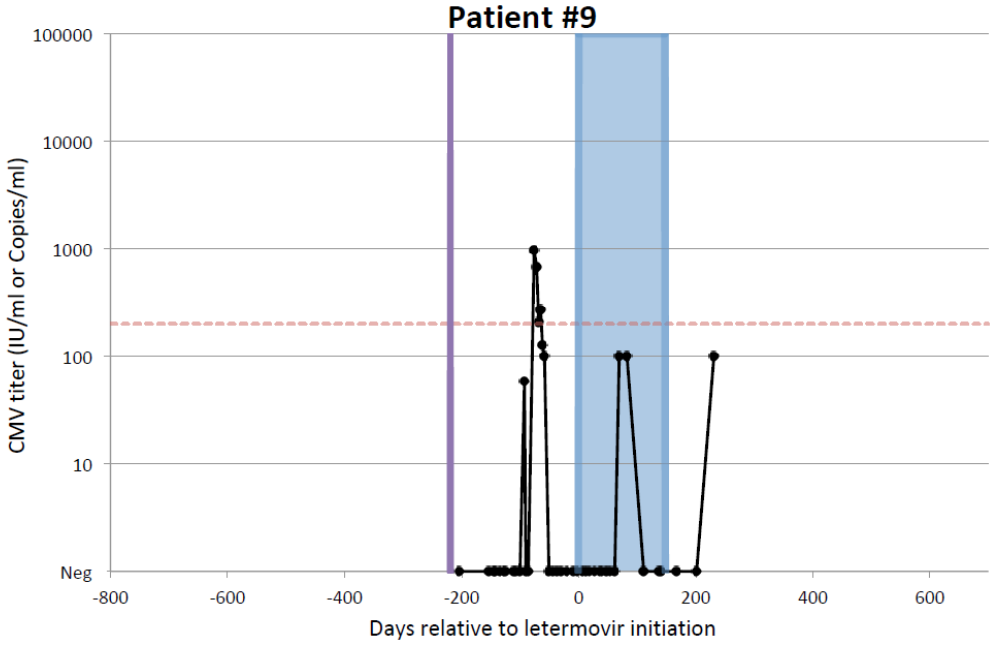
400
600
Days relative to letermovir initiation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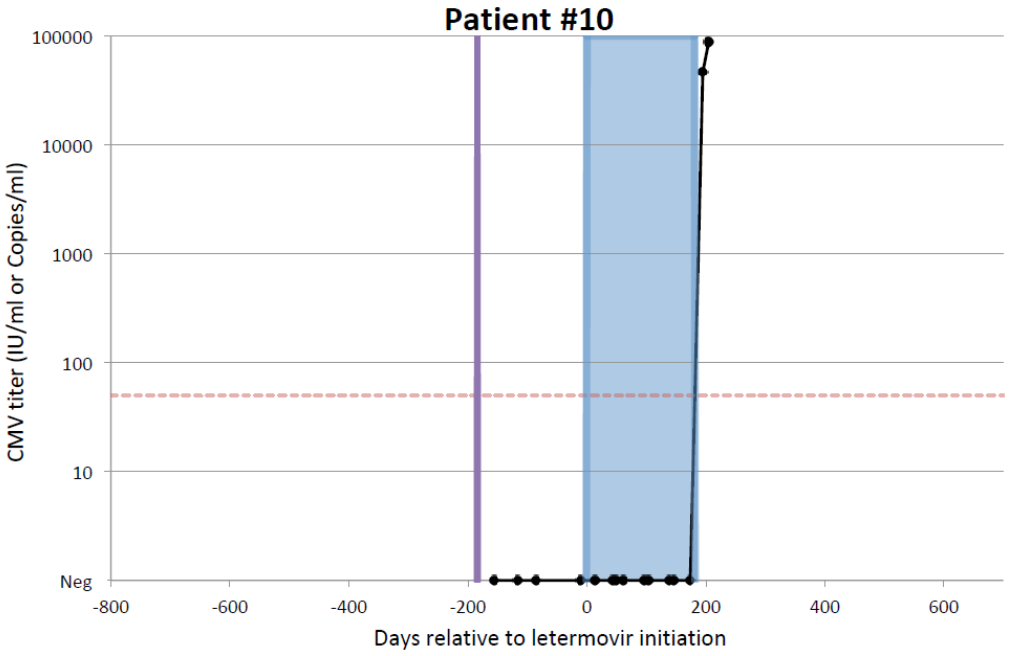
400
600
Days relative to letermovir initiation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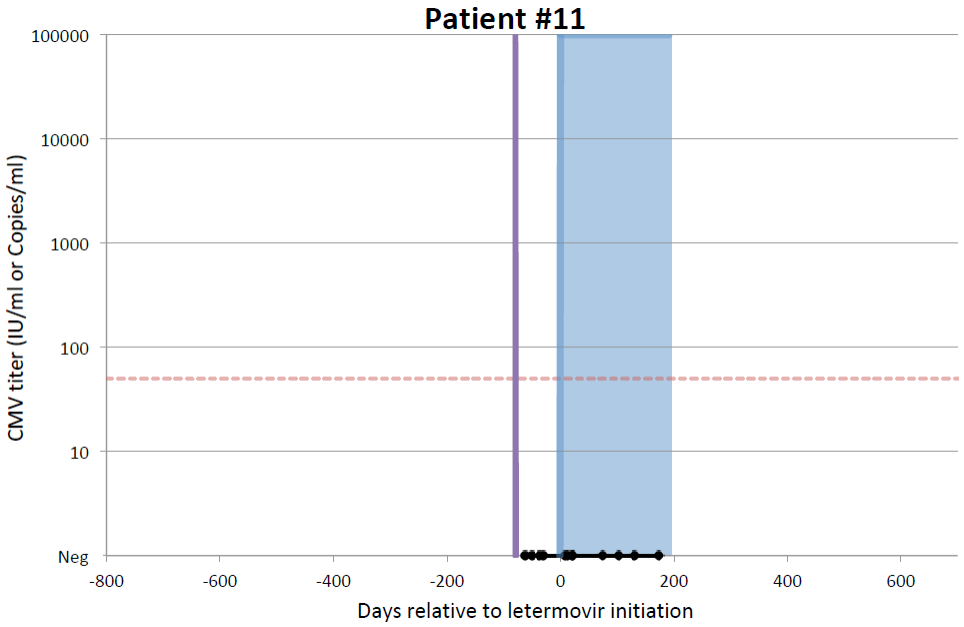
600
Days relative to letermovir initiation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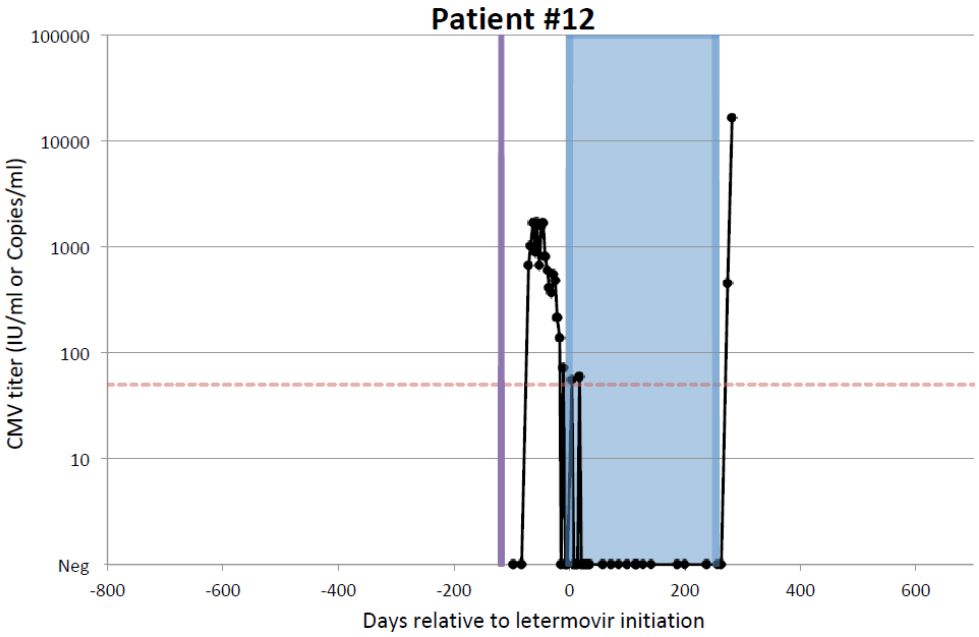
400
600
Days relative to letermovir initiation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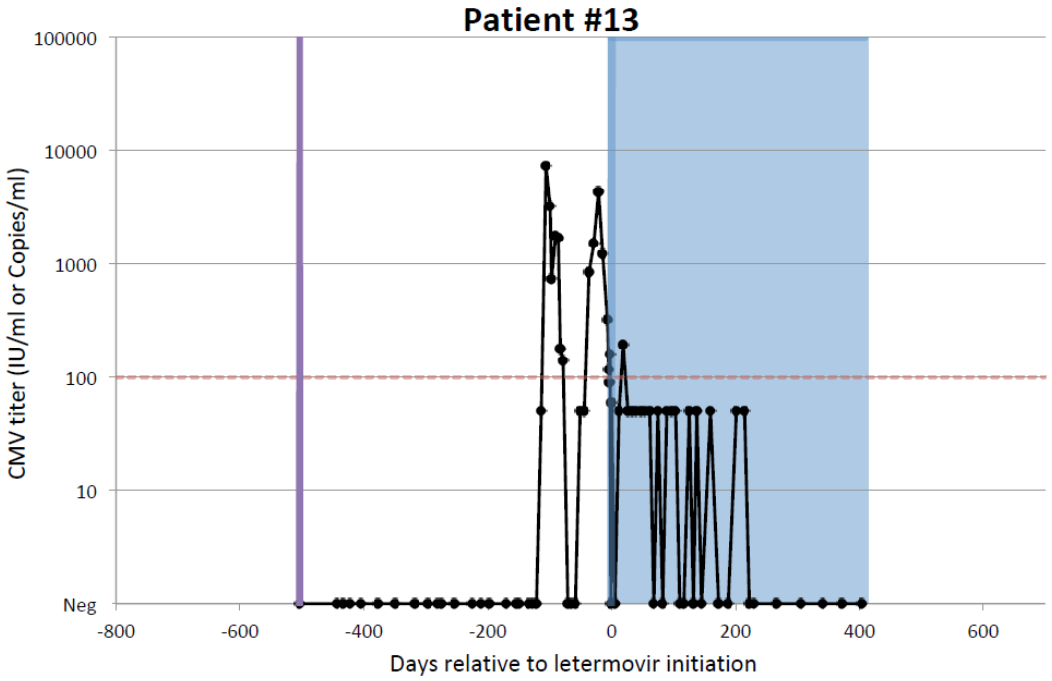
400
600
Days relative to letermovir initiation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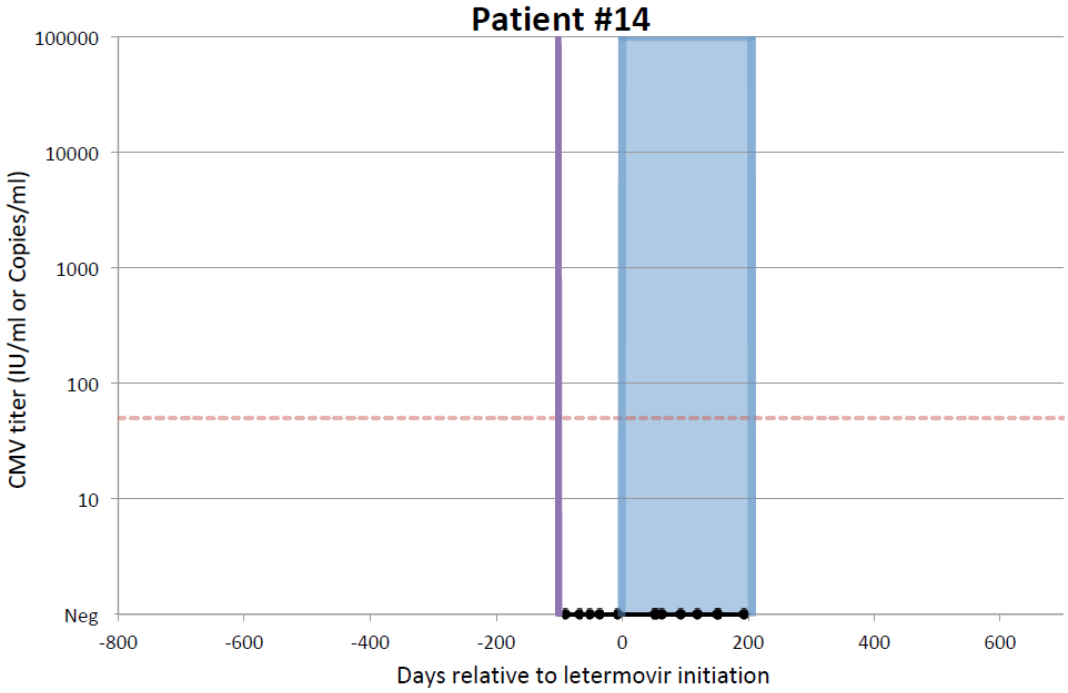
600
Days relative to letermovir initiation


Patient #14
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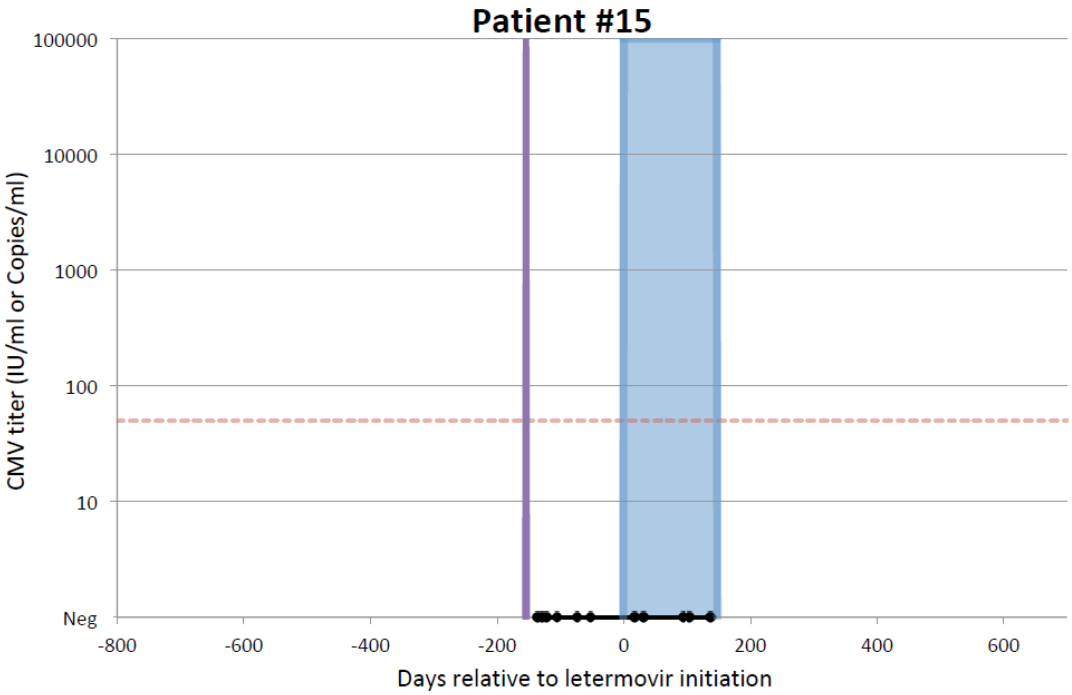
Days relative to letermovir initiation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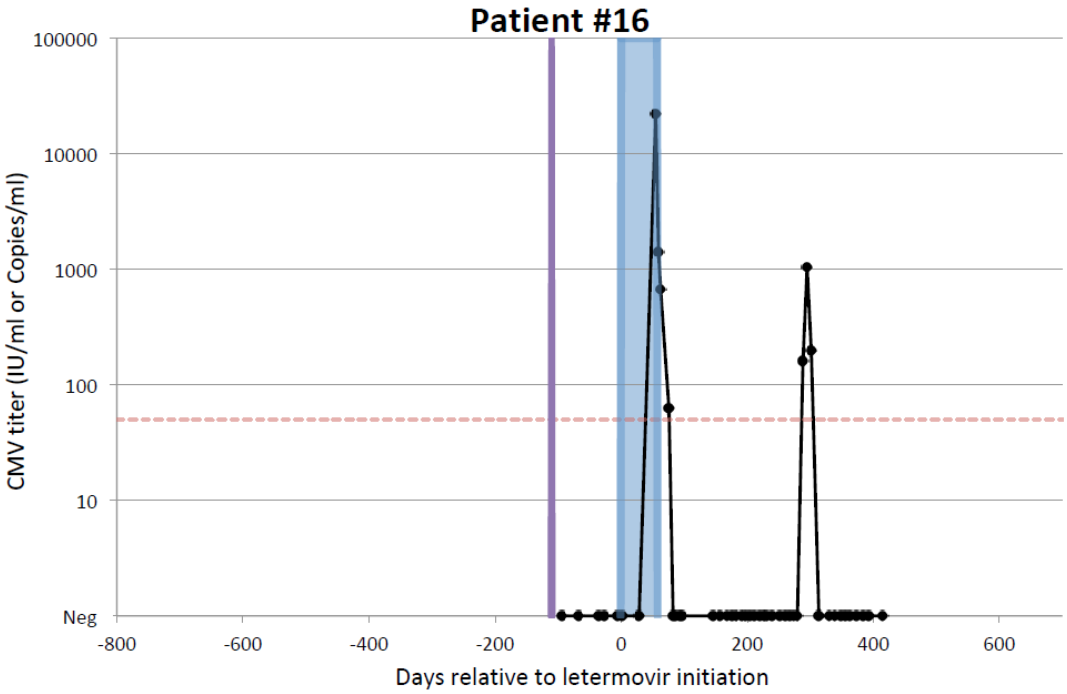
Days relative to letermovir initiation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600
Days relative to letermovir initiation

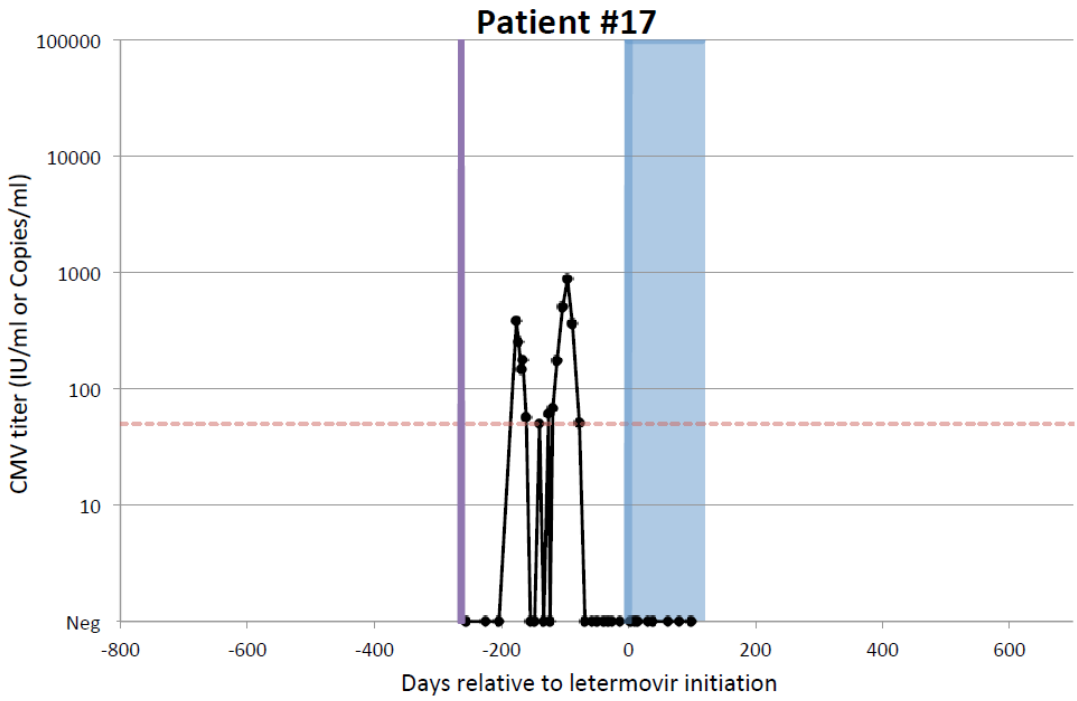

Figure S1. Patient-specific plots of CMV DNAemia from time of transplant through end of study period.